REMARKS

In an Office Action dated October 18, 2002, claims 1-10, 16-19, 26, 30 and 31, all of the claims under consideration in the subject patent application, were rejected. By amendment above, independent claims 1, 16 and 26 have been rewritten. Support for the amendments in claims 1, 16 and 26 can be found on page 1, line 25 of the specification.

Reconsideration of this application and allowance of the claims is respectfully requested in view of the foregoing amendments and the following remarks.

Claims 1-10, 16-19, 26, 30 and 31 were rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The Examiner indicated that it is unclear if the dosage form is formed at a compression force above 80 MPa or if it disintegrates in less than 10 minutes when subjected to a compression force above 80 MPa. Independent claims 1, 16 and 26 have been amended to more clearly define the subject matter of the invention, wherein the dosage form is obtained by compression at a compression force above 80 MPa.

Claims 1-10, 16-19, 26, 30 and 31 have been rejected under 35 U.S.C. § 103(a) as being unpatentable over US 5,380,535 (Greyer et al) in combination with US 4,844,907 (Elgar et al).

The invention of the present application as claimed in claim 1 is directed to a solid non-effervescent compressed dosage form suitable for oral administration and adapted to disintegrate quickly in the gastro-intestinal tract, thereby permitting delivery of high therapeutic levels of ibuprofen (greater than *or* equal to 35% by weight of the composition) to a patient. In particular

this is achieved by including 3 to 20% by weight of an alkali metal (bi)carbonate in the composition.

The inclusion of an alkali metal (bi)carbonate enhances the compressibility of the compressible filler and disintegrant in the pharmaceutical composition of the present invention. Conveniently, this permits a reduction in the amount of compressible filler component that would normally be required in a comparable composition not including an alkali metal (bi)carbonate. Thus, an acceptably sized tablet may be produced which a patient may swallow easily to permit delivery of the ibuprofen medicament to the gastro-intestinal tract.

In addition, unexpectedly the inclusion of an alkali metal (bi)carbonate in the composition of the present invention enables a dosage form to be produced by standard tabletting machines (i.e., at a compression force above 80 MPa), such that the dosage form not only has an acceptable relatively fast disintegration time to permit an on-set hastened action but also exhibits desired hardness so that the dosage forms do not break up during manufacture and during oral administration to a patient. Contrary to the examiner's opinion these parameters are critical to the invention, because in combination they permit the ibuprofen to be delivered to the gastro-intestinal tract and a rapid onset of therapeutic action (see page 1, final paragraph). As stated in the present application, the unexpected finding of improved hardness coupled with desirable disintegration times is contrary to the teaching of the prior art (see page 2, second paragraph).

In contrast to the invention as now claimed, Greyer et al. is directed to providing a completely different solution to a completely different technical problem and thus actively teaches away from the invention of the present application. Greyer et al. is directed to delivering an unpleasant tasting medicament to a patient who has difficulty swallowing a tablet or capsule (see column 1, lines 60 onwards). Greyer et al. solves this problem by providing a chewable composition which disintegrates rapidly in the mouth (see column 2, lines 24 to 26). Greyer et

al. is not concerned whatsoever with providing a hard solid dosage form which when swallowed exhibits a relatively rapid disintegration time in the gastro-intestinal tract.

Suitably, it is most unlikely that a skilled person on reading Greyer et al. would firstly take the non-obvious steps of including a buffering agent in the composition generally disclosed (column 8) or the specific Example 5, then take the next non-obvious step of selecting sodium bicarbonate from a general list of buffering agents, and finally be motivated to compress the mixture in the expectation of forming an acceptably sized dosage form having improved hardness properties so that it may be swallowed easily and then disintegrate relatively rapidly in the gastro-intestinal tract, as Greyer et al. is concerned only with producing chewable dosage forms that disintegrate in the mouth, and thus actively teaches away from forming a solid dosage form which may be swallowed to deliver a medicament to the gastro-intestinal tract.

Moreover, nowhere does Greyer at al teach or suggest that the inclusion of an alkali metal (bi)carbonate would, let alone could, provide an improved compressed dosage form having the claimed hardness and disintegration time, thereby permitting formation of an acceptably sized tablet to allow large doses of ibuprofen to be delivered to the gastro-intestinal tract. Greyer et al. merely mentions at column 6 that sodium bicarbonate is one of a number of buffering agents which may be used to eliminate the burning in the throat caused by ibuprofen i.e., when delivering ibuprofen to the mouth rather than the gastro-intestinal tract.

Furthermore, in Greyer et al. the pharmaceutical composition is in a lipid formulation forming an oral chewable drug delivery system to which may be added a buffering agent such as an alkali metal (bi)carbonate. The current application is directed to a hard tablet exhibiting on-set hastening release in the gastro-intestinal tract, which tablet is obtained through compressing the composition at a compression force of above 80 MPa. Greyer et al. however, do not teach

anything with respect to the compression of the ibuprofen composition or a compression force used to obtain the hard tablet in which the alkali metal (bi)carbonate increases the compressibility and reduces the amount of filler required. Therefore, a skilled person on reading Greyer et al. is not motivated to include an alkali metal (bi)carbonate to produce a hard ibuprofen tablet obtained by compression above 80 MPa, resulting in an on-set hastened ibuprofen release in the gastro-intestinal tract. This deficiency is not cured by Elgar et al, which discloses a pharmaceutical composition in the form of a multi-phase tablet. In Elgar et al. tableting is obtained through a self-lubricating compression aid wherein the self-lubricating compression aid is preferably microcrystalline cellulose, a compound very different than an alkali metal (bi)carbonate as in the present invention. Therefore, Elgar et al. is teaching away from using an alkali metal (bi)carbonate to increase compressibility and reduce filler, allowing compression into a hard tablet or a layer in a pharmaceutical formulation at a compression force of above 80 MPa, as Elgar et al. is teaching the use of microcrystalline cellulose as a compression aid, to compress a pharmaceutical composition into a tablet layer. Thus, Greyer et al. in view of Elgar et al. does not teach or suggest the present invention, but in fact is teaching away from the invention of the current application.

Applicant respectfully submits that the claimed invention in claims 1-10, 16-19, 26, 30 and 31 therefore is not obvious over US 5,380,535 (Greyer et al) in combination with US 4,844,907 (Elgar et al.). Withdrawal of the rejection is respectfully requested.

Claims 1-10, 16-19, 26, 30 and 31 have been rejected under 35 U.S.C. § 103(a) as being unpatentable over US 5,380,535 (Greyer et al) in combination with US 5,262,179 (Gregory et al).

Greyer et al. does not teach or suggest the subject matter of the present invention as discussed above. In addition, Gregory et al. is directed to dry powder water-soluble ibuprofen salts wherein the unpleasant taste is masked by incorporating a taste masking amount of an alkali metal bicarbonate. The disclosure of Gregory et al. is not directed to hard tablets and teaches only the use of alkali metal bicarbonates in dry powder water-soluble ibuprofen. The disclosure in Gregory et al. is silent with respect to the compression into hard tablets of an ibuprofen composition as it is directed to a dry powder, thus effectively teaching away from using these alkali metal bicarbonates in ibuprofen containing hard tablets. The inclusion of these alkali metal (bi)carbonates, increasing the compressibility of the composition of the present invention while reducing the amount of pharmaceutical fillers, enables compression into hard tablets at a compression force of above 80 MPa, forming hard ibuprofen tablets with an on-set hastened release of ibuprofen in the gastro-intestinal tract. These unexpected characteristics of increased compressibility with a reduction of filler and the on-set hastened release in the gastro-intestinal tract of the hard tablet by inclusion of alkali metal (bi)carbonates are not taught or suggested by Gregory et al. Moreover, there is no motivation in Greyer et al. (a chewable tablet dosage form) or in Gregory et al. (a dry powder dosage form) either alone or in combination to compress the composition into a hard ibuprofen tablet with the inclusion of an alkali metal (bi)carbonate as is the subject matter of the present invention. Thus, Greyer et al. in view of Gregory et al. does not teach or suggest the present invention.

Applicant respectfully submits that the claimed invention in claims 1-10, 16-19, 26, 30 and 31 therefore is not obvious over US 5,380,535 (Greyer et al) in combination with US 5,262,179 (Gregory et al). Withdrawal of the rejection is respectfully requested.

Applicant submits that the Examiner's assertion that the current application names joint inventors is incorrect, as Ian A. Price is the sole inventor of the current application. The subject matter of the claims in the present application therefore was solely made by applicant at the time any inventions covered herein were made.

Applicant submits that the present application is now in condition for allowance. Reconsideration and favorable action are earnestly requested.

RESPECTFULLY SUBMITTED,					
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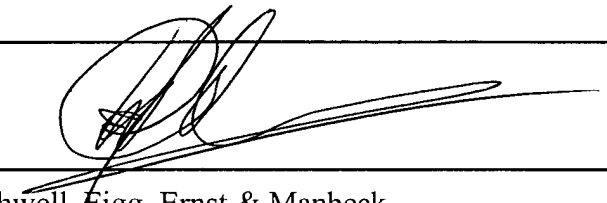
SIGNATURE				DATE	Jan. 21, 2003
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Amended Claims 1, 16 and 26: Version with markings to show changes made

1. (Amended) A solid non-effervescent compressed dosage form suitable for oral administration and adapted to disintegrate quickly in the gastro-intestinal tract comprising a [homogeneous admixture of] racemic ibuprofen medicament present to an extent of 35% or more by weight to the dosage form and in homogeneous admixture with a carrier material comprising

i) a compressible filler component combined with a disintegrating component;

ii) 3-20% solid alkali metal carbonate or bicarbonate by weight of the dosage form;

wherein the dosage form is obtained by compressing said racemic ibuprofen medicament and said carrier material at a compression force above 80 MPa such that said dosage form has a crushing strength in the range 6.5-15 Kp and a disintegration time of less than 10 minutes [at a compression force above 80 MPa], provided that the ibuprofen medicament does not contain a calcium salt of ibuprofen in combination with an alkali metal salt of ibuprofen.

16. (Amended) A method of obtaining an onset-hastened analgesic and/or anti-pyretic response comprising the oral administration of a non-effervescent compressed solid dosage form adapted to disintegrate quickly in the gastro-intestinal tract comprising 35% or more by weight of a racemic ibuprofen medicament in homogeneous admixture with a carrier material comprising

i) a compressible filler component combined with a disintegrating component and

ii) 3-20% solid alkali metal carbonate or bicarbonate by weight of the dosage form,

wherein the dosage form is obtained by compressing said racemic ibuprofen medicament and said carrier material at a compression force above 80 MPa such that said dosage form has a crushing strength in the range 6.5-15 Kp and a disintegration time of less than 10 minutes [at a compression force of above 80 MPa], provided that the ibuprofen medicament does not include a calcium salt of ibuprofen in combination with an alkali metal salt of ibuprofen.

26. (Amended) A solid formulation suitable for oral administration and adapted to disintegrate quickly in the gastro-intestinal tract, said solid formulation having a layer comprising a compressed composition comprising a racemic ibuprofen medicament in homogeneous admixture with a carrier material, the racemic ibuprofen medicament being present to an extent of 35% or more by weight of the composition and the carrier material comprising a compressible filler component combined with a disintegrating component characterised in that the carrier material comprises 3-20% solid alkali metal carbonate or bicarbonate by weight of the dosage form wherein the compressed composition is [capable of compression] obtained by compressing said racemic ibuprofen medicament and said carrier material at a compression force above 80 MPa to provide a layer having a crushing strength in the range 6.5-15 Kp and a disintegration time of less than 10 minutes [at a compression force above 80 MPa].